The hitchhiker antigen: Cause for concern?

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Since antibodies first attained prominence as research reagents in modern biological science labs, researchers have been perplexed as to why one production lot can differ significantly from the next, in terms of performance. Poor antibody performance has caused the loss of countless hours of research, to say nothing of the mental anguish of the researchers themselves. An antigen is a substance that stimulates the production of antibodies.

Now that antibodies are being widely exploited for clinical purposes, the problem of poor antibody performance goes beyond inconvenience to researchers and may threaten patients in a number of ways, including misdiagnosis of disease by pathologists using antibodies to characterize tissue biopsies; disposal of antibody production lots by manufacturers because of the apparent lack of potency; and misinterpretation of research results leading to incorrect conclusions about mechanisms of action for some diseases, which can be costly to pharmaceutical companies pursuing the wrong leads during drug development.

A new article just published in the journal *Biochemistry and Cell Biology* titled: "Hitchhiker antigens: Inconsistent ChIP results, questionable immunohistology data, and poor antibody performance may have a common factor" describes the problem. It claims that antibodies being manufactured today in large biological systems, whether it is a bioreactor filled with mammalian cells or a living organism, such as a rabbit or a goat, may often have a significant proportion of the lot "contaminated" with the very antigens they are designed to target. The antigens contaminating the antibodies can be thought of as "hitchhikers". This is

only a problem if the antibody is designed to target a cellular protein or structure that is already present in the biological system in which it is being made, but such antibodies are increasingly common and are used for research and in medicine.

In this article, the author, Dr. Missag Parseghian, who develops clinical antibodies at Rubicon Biotechnology, introduces readers to a recent survey by the ENCODE consortium of commercial histone-targeting antibodies and how their data highlights the detrimental effects of hitchhiker antigens. His observations may have researchers thinking about the purity of the commercial antibodies sitting in their lab refrigerators. The problem, he says, may be prevalent in a wide array of research areas, not just the areas of chromatin, auto-immune and histone research highlighted here.

"I have been working with antibodies for over 25 years, both as a consumer who uses them in my research and as a scientist working for companies that manufacture them as therapeutics, and what has always struck me about antibodies is the variation in their performance from one lot to the next. Especially when working with antibodies generated from a small research lab and later from a commercial supplier," explained Dr. Parseghian. "Not that one or the other group produces a superior product, rather the same antibody produced by two different groups can show tremendous variation. Understanding and eliminating this variation is critical for successful development of antibody-based biologic agents as drugs."

The article is published online today in *Biochemistry and Cell Biology*.

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